PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:
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UNITED STATES OF AMERICA

PCT

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

REGISTERED

Applicant's or agent's file reference 341.030WO1 .	Date of mailing *(day/month/year)* 22/09/2005
	PAYMENT DUE within **ONE MONTH** from the above date of mailing
International application No. PCT/US2004/031912	International filing date *(day/month/year)* 29/09/2004
Applicant PROMEGA CORPORATION	10/22/05 D- RESP. DUE

1. This International Searching Authority

(i) considers that there are 9 *(number of)* inventions claimed in the international application covered by the claims indicated XXXX/on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated XXXX/on the extra sheet:

(ii) ☒ has carried out a partial international search (see Annex) ☐ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

see annex

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby **invited,** within the time limit indicated above, to pay the amount indicated below:

Fee per additional invention		number of additional inventions		total amount of additional fees
EUR 1.550,00	x	8	=	EUR 12.400
Or,	x		=	

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☒ Claim(s) Nos. see annex have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Joannes Vergoosen

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This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-26, 28-35, 36 partially, 40

   A method for the directional subcloning of DNA fragments comprising: a) providing a first vector comprising a first selectable marker gene and a DNA sequence of interest, which DNA sequence of interest is flanked by at least two restriction enzyme sites (REs), wherein at least one of the flanking RE sites is a site for a first RE which has infrequent restriction sites in cDNAs or open reading frames from at least one species and generates complementary single-strand DNA overhangs, wherein at least one of the flanking RE sites is for a second RE which has infrequent restriction sites in cDNAs or ORFs from at least one species and generates ends that are not complementary to the overhangs generated by the first RE, wherein digestion of the first vector with the first RE and the second RE site generates a first linear DNA fragment which lacks the first selectable marker gene but comprises the DNA sequence of interest; b) providing a second vector comprising a second selectable marker gene which is distinguishable from the first selectable marker gene and non-essential DNA sequences, which non-essential sequences are flanked by at least two restriction enzymes sites, wherein at least one of the flanking RE sites in the second vector is for a third RE which generates complementary single-strand DNA overhangs that are complementary to the single-strand DNA overhang generated by the first restriction enzyme in the first linear DNA fragment, wherein at least one of the flanking RE sites in the second vector is for a fourth RE which generates ends that are not complementary to the ends generated by the first or third RE but can be ligated to the ends generated by the second RE, and wherein digestion of the second vector with the third RE and the fourth RE generates a second linear DNA fragment which lacks non-essential DNA sequences but comprises the second selectable marker, which second linear DNA fragment is flanked by ends which permit the oriented joining of the first linear DNA fragment to the second linear DNA fragment; and c) combining the first and second vectors, the first vector and the second linear DNA fragment, or the second vector and the first linear DNA fragment in a suitable buffer with one or more REs under conditions effective to result in digestion to yield a mixture comprising the first and second linear DNA molecules which are joined in an oriented manner. said method wherein at least one hapaxoterministic RE is used;

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2. claims: 27, 36 partially

A method for producing a vector suitable for expression of an amino acid sequence of interest, comprising: combining at least two vectors in a suitable buffer with one or more restriction enzymes and optionally DNA ligase under conditions effective to result in digestion and optionally ligation to yield a mixture optionally comprising a third vector, wherein a first vector comprises a first selectable marker gene and a DNA sequence of interest, which DNA sequence of interest is flanked by at least two restriction enzyme sites, wherein two or more of the flanking restriction enzyme sites are sites for a first restriction enzyme which is a hapaxoterministic restriction enzyme, wherein digestion of the first vector with the first restriction enzyme generates a first linear DNA fragment which lacks the first selectable marker gene but comprises the DNA sequence of interest and a first pair non-self complementary single-strand DNA overhangs, wherein a second vector comprises a second selectable marker gene which is distinguishable from the first selectable marker gene and non-essential DNA sequences that optionally include a counterselectable gene, which non-essential DNA sequences are flanked by two or more restriction enzyme sites, wherein two or more of the flanking sites in the second vector are for a second restriction enzyme which is a hapaxoterministic restriction enzyme, wherein digestion of the second vector with the second restriction enzyme generates a second linear DNA fragment which lacks non-essential DNA sequences but comprises the second selectable marker gene and a second pair of non-self complementary single-strand DNA overhangs, wherein each of the second pair of the non-self-complementary DNA overhangs is complementary to only one of the single-strand DNA overhangs of the first pair of non-self complementary single-strand DNA overhangs and permits the oriented joining of the first linear DNA fragment to the second linear DNA fragment.

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3. claims: 37-38

A method of inducing expression of a DNA sequence of interest in a host cell, comprising contacting a recombinant host cell which is deficient in rhamnose catabolism, and has a recombinant DNA molecule comprising a rhamnose-inducible promoter operably linked to an open reading frame for a heterologous RNA polymerase, with rhamnose and an expression vector comprising a promoter for the heterologous RNA polymerase operably linked to a DNA sequence of interest.

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4. claim: 39

A method comprising introducing a vector comprising a nucleic acid fragment encoding a barnase which lacks a secretory domain into a recombinant host cell which expresses barstar from a promoter which is constitutively expressed in procaryotic cells.

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5. claims: 41-43

A vector comprising an open reading frame 3' to a DNA fragment of no more than 30 base pairs, which DNA fragment comprise a ribosome binding site, a SgfI recognition site, and a sequence which, when present in mRNA enhances the binding of the mRNA to the small subunit of a eucaryotic ribosome; a vector comprising a SgfI recognition site, a sequence which comprises ATG and which sequence when present in mRNA, enhances the binding of the mRNA to the small subunit of a eucaryotic ribosome, and an open reading frame which begins at the ATG in the sequence;

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6. claims: 44-102, (116-119,121-126,128) partially

A vector comprising a SgfI recognition site 5' to a recognition site for a first restriction enzyme which generates blunt ends; a vector comprising a first open reading frame which includes a SgfI recognition site and a recognition site which is not in the open reading frame for a restriction enzyme that has infrequent restriction sites in cDNAs or open reading frames from at least one species and generates blunt ends; a vector comprising a ribosome binding site which optionally overlaps by one nucleotide with a SgfI recognition site and a recognition site which is not in the open reading frame for a restriction enzyme that has infrequent restriction sites in cDNAs or open reading frames from at least one species and generates blunt ends; a vector comprising a first open reading frame which includes a recognition site for a first restriction enzyme that generates a 3' TA overhang and a recognition site for a second restriction enzyme that is not in the open reading frame generates blunt ends; a support comprising a plurality of recombinant vectors; a process to prepare said support; a library of recombinant cells comprising said recombinant vectors;

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7. claims: 103-114, (116-119,121-126) partially

A vector comprising a first open frame which includes a PmeI recognition site and is llnked at the 5' end by a recognition site for a first restriction enzyme that generates complementary single-strand DNA overhangs; a support comprising a plurality of recombinant vectors, wherein at least one recombinant vector was prepared by using said vector including said PmeI site; a method to prepare said support; a library of recombinant cells comprising said recombinant vectors;

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8. claims: 115,120,127 (121-126,128) partially,129,130

A support comprising a plurality of recombinant vectors, two or more of which comprise an open reading frame for a different polypeptide, wherein at least one recombinant vector comprises a promoter and an open reading frame which is flanked by two exchange site; a method to prepare said support; a library of recombinant cells comprising recombinant vectors or a library of recombinant vectors comprise an open reading frame for a different polypeptide; a method to prepare a plurality of mutagenized recombinant vectors: comprising providing DNAs comprising a plurality of mutagenized open reading frames flanked by two restriction enzyme sites for a first restriction enzyme which is a hapaxoterministic restriction enzyme and generates a first pair of non-self complementary single-stranded DNA overhangs; a library of recombinant cells or a library of recombinant vectors, a plurality of which recombinant vectors comprise said mutagenized recombinant vectors;

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9. claims: 131-141

A method for performing genetic analysis, comprising a) populating a database of genetic data with a plurality of genetic records; b) querying the database of genetic data to identify a first subset of genetic records; wherein each record has at least one recognition site for one predetermined restriction enzyme or for a restriction enzymes included in a set of predetermined restriction enzymes; and c) determining a set of statistics associated with the restriction enzyme recognition sites for at least a second subset of genetic records in the first subset; A computerized system for genetic analysis, comprising a database of genetic data; a processor; a set of one or more programs executed by the processor causing the processor to: query the database of genetic data to identify a first subset of genetic records; wherein each record has at least one recognition site for one predetermined restriction enzyme or for restriction enzymes included in a set of predetermined restriction enzymes, and; determine a set of statistics associated with the restriction enzyme recognition sites for at least a second subset of genetic records in the first subset;

Motivation of lack of unity

Methods of directional cloning of cDNAs by the use single restriction enzymes having a hapaxoterministic recognition site is well known in the prior art. J. Han and W. Rutter describe lambda-gt22S containing two unique in frame SfiI sites positioned in such way that a single cleavage site of the vector by SfiI generates two asymmetric cohesive ends. This vector is suitable for directional cloning of a full-length cDNA library which was generated by a primer adapter strategy for cDNA synthesis, The phage were screened on agar plates, and individual clones were isolated from the phage library, or "mini-prep" lambda DNA templates by the PCR, without subcloning steps (NAR 16:11837,1988). A. Zelenetz and R. Levy described a method of directionally cloning cDNA, by constructing a pair of vectors and devised a cDNA cloning strategy that improves upon previously published methods. The vectors, pLIB:AZ and pLIB:ZA, have two unique (distinct religation specificities; SfiI sites flanking a stuffer fragment which contains the tetracycline-resistance element. These vectors permit the directional cloning of cDNA in both sense (pLIB:AZ) and antisense (pLIB:ZA) orientations relative to the promoter for phage T3 RNA polymerase. cDNA that was synthesized using a primer with a 5' sequence of a SfiI.B site followed by an oligo(dT)16 3' tail was then ligated to an adaptor with the sequence of a SfiI (A) site produced directional molecules that could be cloned into the pLIB vectors (Gene 89, 123-127, 1990).
Furthermore, M Aebi et al. described the directional cloning of the RbetaG sequence inserted as PVuII-BglII fragment into the HincII- and BamHi-cleaved SP64 plasmid, and the cloning of 5'-truncated beta-globin genes by ligating TaqI-BglII fragments into the AccI- and BamHI-cleaved SP64 vectors (Cell 555-565, 1986). Therefore, the directional subcloning of DNA fragments using two different vectors and four different restriction type II enzymes having infrequent restriction sites in said ORF, and generating ends, wherein the first and third restriction enzymes (PvuII and HIincII) and the second and fourth restriction enzymes (BglII and BamHI) can be ligated by combining the second vector with the first linear DNA fragment in a suitable buffer, is already described in the prior art and well known for a man skilled in the art.
Moreover, D. Bilcock et al. and US20030143522 described already vectors, comprising (i) one or more restriction enzyme recognition sites for SgfI, (ii) comprising an ATG sequence, and in addition to SgfI, a restriction enzyme recognition site for an enzyme producing blunt ended DNA. Said vector, once digested with SgfI and said restriction enzyme which generates blunt ends generates a 3'-TA overhang at one site of the DNA fragment and a flush end on the other site (J. Bio. Chem 274, 36379-36386,1999).
WO9102077 describes an efficient cloning system that is particular useful for cloning cDNA copies of eukaryotic mRNAs and can direct the orientation of inserts in plasmid composite rectors with large cloning capacities. A genetic cloning vector comprising at least one replicon; and a site for inserting DNA segments to be cloned that includes at least two non-symmetrical restriction enzyme recognition sequences, wherein at least two of said non-symmetrical restriction enzyme recognition sequences are identical; and the first of said identical restriction enzyme recognition sequences is in the inverted orientation

with respect to a second identical sequence, and said first and second identical restriction enzyme recognition sequences include greater than six positions having invariable DNA base pairs. Moreover, WO0107633 described a method for directional insertion of DNA, comprising providing a recipient DNA vector having a restriction site which contains a degenerate recognition sequence and which generates cohesive ends when digested with its corresponding restriction endonuclease (RE), and digesting recipient DNA vector with RE corresponding to the restriction site, generating two cohesive ends on the digested vector.

In the light of the prior art, the first problem of underlying application can be defined as the provision of an alternative method of directional subcloning of DNA fragments.

The first solution as described and claimed can be summarized: -A method for the directional subcloning of DNA fragments comprising: a) providing a first vector comprising a first selectable marker gene and a DNA sequence of interest, which DNA sequence of interest is flanked by at least two restriction enzyme sites (REs), wherein at least one of the flanking RE sites is a site for a first RE which has infrequent restriction sites in cDNAs or open reading frames from at least one species and generates complementary single-strand DNA overhangs, wherein at least one of the flanking RE sites is for a second RE which has infrequent restriction sites in cDNAs or ORFs from at least one species and generates ends that are not complementary to the overhangs generated by the first RE, wherein digestion of the first vector with the first RE and the second RE site generates a first linear DNA fragment which lacks the first selectable marker gene but comprises the DNA sequence of interest; b) providing a second vector comprising a second selectable marker gene which is distinguishable from the first selectable marker gene and non-essential DNA sequences, which non-essential sequences are flanked by at least two restriction enzymes sites, wherein at least one of the flanking RE sites in the second vector is for a third RE which generates complementary single-strand DNA overhangs that are complementary to the single-strand DNA overhang generated by the first restriction enzyme in the first linear DNA fragment, wherein at least one of the flanking RE sites in the second vector is for a fourth RE which generates ends that are not complementary to the ends generated by the first or third RE but can be ligated to the ends generated by the second RE, and wherein digestion of the second vector with the third RE and the fourth RE generates a second linear DNA fragment which lacks non-essential DNA sequences but comprises the second selectable marker, which second linear DNA fragment is flanked by ends which permit the oriented joining of the first linear DNA fragment to the second linear DNA fragment; and c) combining the first and second vectors, the first vector and the second linear DNA fragment, or the second vector and the first linear DNA fragment in a suitable buffer with one or more REs under conditions effective to result in digestion to yield a mixture comprising the first and second linear DNA molecules which are joined in an oriented manner. said method wherein at least one hapaxoterministic RE is used;

The second solution as described and claimed can be summerized: A method for producing a vector suitable for expression of an amino acid sequence

of interest, comprising:
combining at least two vectors in a suitable buffer with one or more restriction enzymes and optionally DNA ligase under conditions effective to result in digestion and optionally ligation to yield a mixture optionally comprising a third vector, wherein a first vector comprises a first selectable marker gene and a DNA sequence of interest, which DNA sequence of interest is flanked by at least two restriction enzyme sites, wherein two or more of the flanking restriction enzyme sites are sites for a first restriction enzyme which is a hapaxoterministic restriction enzyme, wherein digestion of the first vector with the first restriction enzyme generates a first linear DNA fragment which lacks the first selectable marker gene but comprises the DNA sequence of interest and a first pair non-self complementary single-strand DNA overhangs, wherein a second vector comprises a second selectable marker gene which is distinguishable from the first selectable marker gene and non-essential DNA sequences that optionally include a counterselectable gene, which non-essential DNA sequences are flanked by two or more restriction enzyme sites, wherein two or more of the flanking sites in the second vector are for a second restriction enzyme which is a hapaxoterministic restriction enzyme, wherein digestion of the second vector with the second restriction enzyme generates a second linear DNA fragment which lacks non-essential DNA sequences but comprises the second selectable marker gene and a second pair of non-self complementary single-strand DNA overhangs, wherein each of the second pair of the non-self-complementary DNA overhangs is complementary to only one of the single-strand DNA overhangs of the first pair of non-self complementary single-strand DNA overhangs and permits the oriented joining of the first linear DNA fragment to the second linear DNA fragment.

In the light of the prior art, the second problem of underlying application can be defined as the provision of an alternative method of inducing expression of a DNA sequence of interest in a host cell.
The solution as described and claimed can be summarized: contacting a recombinant host cell which is deficient in rhamnose catabolism, and has a recombinant DNA molecule comprising a rhamnose-inducible promoter operably linked to an open reading frame for a heterologous RNA polymerase, with rhamnose and an expression vector comprising a promoter for the heterologous RNA polymerase operably linked to a DNA sequence of interest.

In the light of the prior art, the third problem of underlying application can be defined as the provision of a further plasmid with positive selection and cloning based on a conditionally lethal gene.
The solution as described and claimed can be summarized: -A method comprising introducing a vector comprising a nucleic acid fragment encoding a barnase which lacks a secretory domain into a recombinant host cell which expresses barstar from a promoter which is constitutively expressed in procaryotic cells.

In the light of the prior art, the fourth problem of underlying application can be seen in providing alternative vectors comprising a single restriction enzyme type II site.

The solution as described and claimed can be summarized: -A vector comprising an open reading frame 3' to a DNA fragment of no more than 30 base pairs, which DNA fragment comprise a ribosome binding site, a SgfI recognition site, and a sequence which, when present in mRNA enhances the binding of the mRNA to the small subunit of a eucaryotic ribosome; a vector comprising a SgfI recognition site, a sequence which comprises ATG and which sequence when present in mRNA, enhances the binding of the mRNA to the small subunit of a eucaryotic ribosome, and an open reading frame which begins at the ATG in the sequence;

In the light of the prior art, the fifth problem of underlying application can be seen in providing alternative vectors comprising a single restriction enzyme type II site 5' to a recognition site for a first restriction enzyme which generates blunt ends.
The solution as described and claimed can be summarized: -A vector comprising a SgfI recognition site 5' to a recognition site for a first restriction enzyme which generates blunt ends; a vector comprising a first open reading frame which includes a SgfI recognition site and a recognition site which is not in the open reading frame for a restriction enzyme that has infrequent restriction sites in cDNAs or open reading frames from at least one species and generates blunt ends; a vector comprising a ribosome binding site which optionally overlaps by one nucleotide with a SgfI recognition site and a recognition site which is not in the open reading frame for a restriction enzyme that has infrequent restriction sites in cDNAs or open reading frames from at least one species and generates blunt ends; a vector comprising a first open reading frame which includes a recognition site for a first restriction enzyme that generates a 3' TA overhang and a recognition site for a second restriction enzyme that is not in the open reading frame generates blunt ends; a support comprising a plurality of recombinant vectors; a process to prepare said support; a library of recombinant cells comprising said recombinant vectors;

In the light of the prior art, the sixth problem of underlying application can be seen in providing alternative vectors comprising a "blunt ended" single restriction enzyme type II site, and is flanked at the 5' end by a restriction enzyme for a first restriction endonuclease.
The solution as described and claimed can be summarized: -A vector comprising a first open frame which includes a PmeI recognition site and is llnked at the 5' end by a recognition site for a first restriction enzyme that generates complementary single-strand DNA overhangs; a support comprising a plurality of recombinant vectors, wherein at least one recombinant vector was prepared by using said vector including said PmeI site; a method to prepare said support; a library of recombinant cells comprising said recombinant vectors;

In the light of the prior art, the seventh problem of underlying application can be seen in providing a support of alternative recombinant vectors comprising a promoter and an open reading frame.
The solution as described and claimed can be summarized: -A support comprising a plurality of recombinant vectors, two or more of which comprise an open reading frame for a different polypeptide, wherein at

least one recombinant vector comprises a promoter and an open reading frame which is flanked by two exchange site; a method to prepare said support; a library of recombinant cells comprising recombinant vectors or a library of recombinant vectors comprise an open reading frame for a different polypeptide; a method to prepare a plurality of mutagenized recombinant vectors: comprising providing DNAs comprising a plurality of mutagenized open reading frames flanked by two restriction enzyme sites for a first restriction enzyme which is a hapaxoterministic restriction enzyme and generates a first pair of non-self complementary single-stranded DNA overhangs; a library of recombinant cells or a library of recombinant vectors, a plurality of which recombinant vectors comprise said mutagenized recombinant vectors;

In the light of the prior art, the eighth problem of underlying application can be seen in providing an alternative method for performing genetic analysis.
The solution as described and claimed can be summarized: -A method for performing genetic analysis, comprising a) populating a database of genetic data with a plurality of genetic records; b) querying the database of genetic data to identify a first subset of genetic records; wherein each record has at least one recognition site for one predetermined restriction enzyme or for a restriction enzymes included in a set of predetermined restriction enzymes; and c) determining a set of statistics associated with the restriction enzyme recognition sites for at least a second subset of genetic records in the first subset; A computerized system for genetic analysis, comprising a database of genetic data; a processor; a set of one or more programs executed by the processor causing the processor to: query the database of genetic data to identify a first subset of genetic records; wherein each record has at least one recognition site for one predetermined restriction enzyme or for restriction enzymes included in a set of predetermined restriction enzymes, and; determine a set of statistics associated with the restriction enzyme recognition sites for at least a second subset of genetic records in the first subset.

In the view of the fact that methods for directional cloning are known; due to the fact that vectors for the directional cloning of multiple DNA sequences are already known, furthermore, due to the fact that vectors comprising a SgfI recognition site 5’ to a recognition site for a first restriction enzyme which generates blunt ends are state of the art, and libraries of recombinant cells comprising recombinant vectors or a library of recombinant vectors are known, and moreover alternative methods of preparing a support comprising a plurality of recombinant vectors are well known, due to essential difference of the eight problems and at least nine different solutions and due to the fact that no other technical features can be distinguished which, in the light of the prior art, could be regarded as special technical features common to these solutions, the ISA is of the opinion that there is no single inventive concept underlying the plurality of claimed inventions of the present application in the sense of 13.1 PCT. Consequently there is lack of unity and different inventions, not belonging to a common inventive concept are formulated as the different subjects on the communication pursuant to Art. 17(3)(a), PCT.

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US2004/031912

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.
3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.
4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	AEBI M ET AL: "Sequence requirements for splicing of higher eukaryotic nuclear pre-mRNA." CELL. 21 NOV 1986, vol. 47, no. 4, 21 November 1986 (1986-11-21), pages 555-565, XP008052167 ISSN: 0092-8674 page 563, right-hand column, paragraph 2	1-5, 14-18,26
X	ZELENETZ A D ET AL: "DIRECTIONAL CLONING OF CDNA USING A SELECTABLE SFII CASSETTE" GENE, ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, NL, vol. 89, no. 1, 1990, pages 123-127, XP001019191 ISSN: 0378-1119 abstract	14
X	HAN J H ET AL: "LAMBDAGT22S, A PHAGE EXPRESSION VECTOR FOR THE DIRECTIONAL CLONING OF CDNA BY THE USE OF A SINGLE RESTRICTION ENZYME SFII" NUCLEIC ACIDS RESEARCH, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 16, no. 24, 1988, page 11837, XP001026354 ISSN: 0305-1048 the whole document	14

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

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Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US2004/031912

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BILCOCK DENZIL T ET AL: "Reactions of type II restriction endonucleases with 8-base pair recognition sites" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 51, 17 December 1999 (1999-12-17), pages 36379-36386, XP002194222 ISSN: 0021-9258 the whole document -----	1-36,40
A	US 5 391 487 A (KAPPELMAN ET AL) 21 February 1995 (1995-02-21) the whole document -----	1-36,40
A	KAPPELMAN J R ET AL: "SgfI, a new type-II restriction endonuclease that recognizes the octanucleotide sequence 5'-GCGATCGC-3'" GENE, ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, NL, vol. 160, no. 1, 4 July 1995 (1995-07-04), pages 55-58, XP004042177 ISSN: 0378-1119 the whole document -----	1-36,40
A	US 2003/143522 A1 (PERLER FRANCINE B ET AL) 31 July 2003 (2003-07-31) page 8, right-hand column, line 38 - page 9, right-hand column, line 2 -----	1-36,40
A	WO 01/07633 A (THE UNITED STATES OF AMERICA, AS REPRESENTED BY THE SECRETARY OF AGRIC) 1 February 2001 (2001-02-01) the whole document -----	1-36,40
A	WO 91/02077 A (THE UNITED STATES OF AMERICA, REPRESENTED BY THE S) 21 February 1991 (1991-02-21) the whole document -----	1-36,40
A	BERGER S L: "Gene modification with hapaxoterministic restriction enzymes. Easing the way." METHODS IN MOLECULAR BIOLOGY (CLIFTON, N.J.) 2001, vol. 160, 2001, pages 443-458, XP008052201 ISSN: 1064-3745 the whole document -----	1-36,40

7

Patent Family Annex

Information on patent family members

International Application No
PCT/US2004/031912

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5391487 A	21-02-1995	NONE	
US 2003143522 A1	31-07-2003	US 2002142296 A1	03-10-2002
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		EP 0773294 A2	14-05-1997
		JP 7255491 A	09-10-1995
		JP 4503309 T	18-06-1992
		WO 9102077 A1	21-02-1991
		US 5595895 A	21-01-1997